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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,936	08/30/2001	Brigitte Bathe	32301WD202	6329
441	7590	07/28/2004	EXAMINER	
SMITH, GAMBRELL & RUSSELL, LLP 1850 M STREET, N.W., SUITE 800 WASHINGTON, DC 20036			KERR, KATHLEEN M	
			ART UNIT	PAPER NUMBER

1652

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/941,936

Applicant(s)

BATHE ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14, 16-18, 21, 25-29, 33 and 34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14, 16-18, 21, 26, 27 and 33 is/are allowed.
- 6) ☒ Claim(s) 25, 28, 29 and 34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on March 10, 2004), Applicants filed a response and amendment received on June 10, 2004. Said amendment amended Claims 14, 18, 21, 25, 26, 28, and 29 and added new Claims 33 and 34. Thus, Claims 14, 16-18, 21, 25-29 and 33-34 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign application 10043332.4 filed in Germany on September 2, 2000 and application 10033426.5 filed in Germany on July 10, 2001. Translations of said documents have been received on December 23, 2003.

Withdrawn - Objections to the Specification

3. Previous objection to the Abstract for not completely describing the disclosed subject matter is withdrawn by virtue of Applicant's amendment to the specification.

Withdrawn - Claim Rejections - 35 U.S.C. § 112, second paragraph

4. Previous rejection of Claims 14, 16-18, 21, and 25-29 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicant's amendment removing limitations to RNA polymerase sigma factor C activity.

5. Previous rejection of Claims 25 and 26 under 35 U.S.C. § 112, second paragraph, as being indefinite for various additional genes and proteins as follows: “a protein for lysine export”, “a Zwa1 protein”, and “a Zwa2 protein”, is withdrawn in part as relating to gene names and all except “zwa1 protein” by virtue of Applicant’s amendment. See below for maintenance of rejection for remaining issue.

6. Previous rejection of Claim 28 under 35 U.S.C. § 112, second paragraph, as being indefinite for the nature of the vector used is withdrawn by virtue of Applicant’s amendment.

Maintained - Claim Rejections - 35 U.S.C. § 112, second paragraph

7. Previous rejection of Claim 25 under 35 U.S.C. § 112, second paragraph, as being indefinite for “a Zwa1 protein” is maintained. Applicant’s arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that the zwa1 protein is well known in the art by virtue of its disclosure in USPN 6,632,644. The Examiner disagrees. USPN 6,632,644 teaches a single example of what the inventors name as zwa1, said example being from *C. glutamicum*. No genus is described in the patent so that one of skill in the art would be able to recognize such as genus, as required for the language of instant Claim 25. No function of the species of zwa1 is disclosed in USPN 6,632,644 so that one of skill in the art might be able to glean characteristics of a genus of zwa1 proteins from the disclosure. Thus, the nature of a gene encoding any zwa1 protein, as required for the genus in Claim 25, is unclear.

Applicant also argues that the *zwa1* protein is clearly described by virtue of its incorporation by reference of DE 19959328.0, which clearly describes the *zwa1* protein. The Examiner disagrees for the reasons stated above with respect to USPN 6,632,644.

Withdrawn - Claim Rejections - 35 U.S.C. § 112, first paragraph

8. Previous rejection of Claim 25 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known feedback-resistance aspartate kinase and threonine dehydratase, does not reasonably provide enablement for methods using unknown feedback-resistance aspartate kinase and threonine dehydratase, is withdrawn by virtue of Applicant's amendment deleting this limitation.

9. Previous rejection of Claim 25 under 35 U.S.C. § 112, first paragraph, written description, relating to methods using genes for feedback-resistant aspartate kinase and feedback-resistant threonine dehydratase is withdrawn by virtue of Applicant's amendment deleting these limitations.

10. Previous rejection of Claims 25 and 26 under 35 U.S.C. § 112, first paragraph, written description, for using genes encoding a protein for lysine export and *Zwa2* protein is withdrawn by virtue of Applicant's amendment deleting these limitations.

11. Previous rejection of Claims 14, 16-18, 21, and 25-29 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1 by transforming a host cell with a vector comprising SEQ ID

NO:1 and a promoter, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the specification, is withdrawn by virtue of Applicant's amendment to the claims limiting overexpression to increasing copy number and/or inserting a promoter, both of which are enabled by the state of the art.

12. Previous rejection of Claims 25-26 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known *zwa1*, *zwa2*, and *lysC* genes as described in the specification, does not reasonably provide enablement for methods using other of these genes, is withdrawn in part with respect to *zwa2* and *lysC* by virtue of Applicant's removal of these limitations from the claims.

Maintained - Claim Rejections - 35 U.S.C. § 112, first paragraph

13. Previous rejection of Claim 25 under 35 U.S.C. § 112, first paragraph, written description, for using genes that encode a *Zwa1* protein is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that the *zwa1* protein is adequately described by virtue of its disclosure in DE 19959328.0, which document is incorporated by reference. The Examiner disagrees. While said document adequately describes a species of *zwa1* protein, that is the *zwa1* protein from *C. glutamicum*, it is inadequate to support the genus, as claimed. Specifically for Claim 25 the Examiner previously noted the contrast of using named enzymes as follows:

“While genes encoding known enzymes with particular functions, such as genes encoding dihydrodipicolinate synthase, are adequately described by virtue of their specification function and their examples in the art, this is not the case for genes encoding proteins without clear support in the art for their genus: ... *Zwa1* protein.... The mere name of these proteins does NOT connote a structure and/or

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function as is the case with the specific enzymes noted elsewhere in the claims. One example of each is noted in the specification; however, no description of how to maintain Zwa1-like protein structure and/or function is found. Thus, one of skill in the art would be unable to predict the structure of other members of the genus of genes claimed.”

For these reasons, description of a single example of a *zwa1* gene does not adequately support the claimed genus.

14. Previous rejection of Claim 25 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known *zwa1*, genes as described in the specification, does not reasonably provide enablement for methods using other of these genes, is maintained. Applicant’s arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that previous remarks with respect to clarity and written description obviate the enablement rejection with respect to the *zwa1* gene. The Examiner disagrees for the reasons noted above in disagreement of Applicant’s arguments against the rejections under 35 U.S.C. § 112, second paragraph, as well as 35 U.S.C. § 112, first paragraph, written description. To practice the claimed methods to the full extent of their scope, one of skill in the art must be able to overexpress any *zwa1* protein in coryneform. While one of skill in the art would be able to overexpress *the* *zwa1* protein described in USPN 6,632,644, DE 19959328.0, and the instant application (by reference), overexpressing any *zwa1* protein is not enabled because to do so would require undue experimentation as noted in the previous Office action.

15. Previous rejection of Claims 28-29 under 35 U.S.C. § 112, first paragraph, enabling deposit, is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the amendment to the specification to include the full address of the depository is sufficient to overcome the rejection; the Examiner disagrees.

As previously noted, "To practice the instant methods, one of skill in the art is required to use DH5 α mcr/pEC-XK99EsigCb2ex or DSM5715/pEC-XK99E. While the instant specification contains limited deposit information on page 19, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit of DSM 12968, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and **full address** of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), **and (5)** the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative."

While above item (4) has been fulfilled, above item (5) has not. Therefore, the rejection is maintained herein.

NEW ISSUES

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claim 34 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "having an RNA polymerase sigma-C factor" at the end of the claim is confusing as to its form and definition. Is the polypeptide meant to have this activity? If so, what activity since the factor is a protein, not an enzyme with an enzymatic activity to claim? Moreover, it is unclear as to just what limitation it imparts since SEQ ID NO:1 is invariable and inherently encodes SEQ ID NO:2, which is disclosed as an RNA polymerase sigma-C factor. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claim 34 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1 by transforming a host cell with a vector comprising SEQ ID NO:1 and a promoter, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the

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specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the specification on page 12 (paragraph [0038]), means of overexpression are described. Said means include not only increasing the copy number of a gene or regulating the gene with a particular promoter, which means are enabled by the art, but also include altering the

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ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions, all of which are known in the art to “overexpress” a gene in specific examples, but none of which are predictable with sigC or other genes that lack specific examples in the art. The specification provides no working examples or direction for overexpression using means of ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions. The nature of the invention is that these means are specific to a particular gene sequence and cannot be extrapolated from other, unrelated genes; there is no particular recipe of media that will overexpress all genes. Thus, overexpression using these methods is wholly unpredictable and not enabled by the specification or the art.

On page 9 of Applicant’s remarks, rebuttal of this rejection (although the claim referred to is new claim 33, which is incorrect) is presented since this rejection was set forth against previously pending claim. Applicant’s arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that experimentation required to “overexpress” the sigC would not be undue and that detailing some of the methods of overexpression is sufficient. While the Examiner agrees that the specification need not expressly describe every permutation of the claimed methods, one of skill in the art must be able to perform said methods to the extent that they are claimed without undue experimentation. Since the specification specifically encompasses methods such as altering the lifetime of the sigC mRNA or altering the protein to resist degradation within the scope of the claimed invention, such examples must be within the skill of the art. As noted above, they are not. Thus, the instant rejection is herein applied to Claim 34, which mirrors previous Claim 14.

Summary of Issues

18. The following is a summary of the issues remaining in the instant application:
- a) Claim 25 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for “a Zwa1 protein”.
 - b) Claim 34 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase “having an RNA polymerase sigma-C factor”.
 - c) Claim 25 stands rejected under 35 U.S.C. § 112, first paragraph, written description, for using genes that encode a Zwa1 protein.
 - d) Claim 25 stands rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known zwa1, genes as described in the specification, does not reasonably provide enablement for methods using other of these genes.
 - e) Claims 28-29 stand rejected under 35 U.S.C. § 112, first paragraph, enabling deposit.
 - f) Claim 34 stands rejected under 35 U.S.C. § 112, first paragraph, scope of enablement (overexpression).

Conclusion

19. Claims 14, 16-18, 21, 26, 27 and 33 are allowed in the Office action; Claims 25, 28, 29, and 34 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R.

§ 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Examiner
Art Unit 1652

July 26, 2004